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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/018,695 | 06/26/2002 | Nathalie Garcon | B45186 | 7784 |

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EXAMINER

PARKIN, JEFFREY S

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| ART UNIT | PAPER NUMBER |
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1648

DATE MAILED: 12/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.



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| SERIAL NUMBER | FILING DATE | FIRST NAMED APPLICANT | ATTORNEY DOCKET NO. |
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| EXAMINER | |
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| ART UNIT | PAPER NUMBER |
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DATE MAILED:

Please find below a communication from the EXAMINER in charge of this application
Commissioner of Patents

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth below. Applicants are reminded that **all** amino acid sequences located in the specification (including the text of the specification, figures, figure descriptions, tables, and claims) that fall under the aforementioned guidelines must reference the appropriate sequence identifier (SEQ ID NO.:). The specification recites various nucleotide sequences on pp. 4 and 5 (e.g., WD1001) that do not have sequence identifiers. Applicants should carefully review the claims and specification for compliance. Applicants are advised that the claims and specification should be amended where necessary to reflect this requirement. Any questions regarding compliance with the sequence rules requirements specifically should be directed to the departments listed at the bottom of the Notice to Comply.

APPLICANT IS GIVEN ONE MONTH FROM THE DATE OF THIS LETTER WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 C.F.R. §§ 1.821-1.825. Failure to comply with these requirements will result in **ABANDONMENT** of the application under 37 C.F.R. § 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, James C. Housel, can be reached at (571) 272-0902. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Formal communications may be submitted through the official facsimile number which is (703) 872-9306. Hand-carried formal communications should be directed toward the customer window located in Crystal Plaza Two, 2011 South Clark Place, Arlington, VA. Applicants are directed toward the O.G. Notice for further guidance. 1280 O.G. 681. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,



Jeffrey S. Parkin, Ph.D.
Primary Examiner
Art Unit 1648

12 December, 2004

Particularly preferred vaccines according to the invention comprise an HIV fusion protein such as Nef-Tat and optionally an additional HIV protein. Particularly preferred in a vaccine formulation according to the invention is a combination of an HIV fusion protein plus gp120, more particularly Nef-Tat with gp120.

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Derivatives encompassed within the present invention also include mutated proteins. The term 'mutated' is used herein to mean a molecule which has undergone deletion, addition or substitution of one or more amino acids using well known techniques for site directed mutagenesis or any other conventional method.

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Vaccine preparation is generally described in Vaccine Design - The subunit and adjuvant approach (Ed. Powell and Newman) Pharmaceutical Biotechnology Vol. 6 Plenum Press 1995. Encapsulation within liposomes is described by Fullerton, US Patent 4,235,877.

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The preferred oligonucleotides preferably contain two or more CpG motifs separated by six or more nucleotides. The oligonucleotides of the present invention are typically deoxynucleotides. In a preferred embodiment the internucleotide in the oligonucleotide is phosphorodithioate, or more preferably a phosphorodithioate bond, although phosphodiester and other internucleotide bonds are within the scope of the invention including oligonucleotides with mixed internucleotide linkages.

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Preferred oligonucleotides have the following sequences:

| Oligo (internal designation*) | 5'-SEQUENCE-3' | CpG | Thio |
|-------------------------------|-----------------------------------|-----|------|
| WD1001 | TCC ATG ACG TTC CTG ACG TT | + | + |
| WD1002 | TCT CCC AGC GTG CGC CAT | + | + |
| WD1003 | ACC GAT AAC GTT GCC GGT GAC G | + | - |
| WD1004 | G*G*G GTC AAC GTT GAG* G*G*G* G*G | + | Mix |
| WD1005 | TCC ATG AGC TTC CTG AGC TT | - | + |

| | | | |
|--------|---|---|---|
| WD1006 | TCC ATG ACG TTC CTG ACG TT | + | - |
| WD1007 | ACC GAT GAC GTC GCC GGT GAC GGC ACC ACG | + | + |
| | TCG TCG TTT TGT CGT TTT GTC GTT | + | + |

* alternatively referred to as WD001-WD007

In the above table a + in the Thio column indicates the presence of a thioate modification. 'Mix' indicates a mixture of thioate modification and sequence without thioate modification (the asterisks indicate the linkages with a thioate modification). A - in the Thio column indicates absence of a thioate modification. A + in the CpG column indicates a the presence of a CpG motif and a - in the CpG column indicates absence of a CpG motif. For example WD1005 contains a GpC rather than a CpG motif, thus it is marked with a - in the CpG column of the table. WD1007 contains a palindromic motif (GACGTC) as well as other non-palindromic CpG sequences. This is also within the scope of a CpG oligonucleotide as the term is used in the present application.

The CpG oligonucleotides utilised in the present invention may be synthesized by any method known in the art (eg EP 0 468 520). Conveniently, such oligonucleotides may be synthesized utilising an automated synthesizer. Methods for producing phosphorothioate oligonucleotides or phosphorodithioate are described in US 5,666,153, US 5,278,302 and WO 95/26204.

The amount of protein in each vaccine dose is selected as an amount which induces an immunoprotective response without significant, adverse side effects in typical vaccinees. Such amount will vary depending upon which specific immunogen is employed and how it is presented. Generally, it is expected that each dose will comprise 1-1000 µg of protein, preferably 2-500 µg, most preferably 5-250 µg. An optimal amount for a particular vaccine can be ascertained by standard studies involving observation of appropriate immune responses in subjects. Following an initial vaccination, subjects may receive one or several booster immunisations adequately spaced.

Application No.: 10/018695

**NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING
NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES**

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- ☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.
- ☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- ☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- ☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- ☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- ☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- ☒ 7. Other: see correspondence

May Need To
Applicant ~~Must~~ Provide:

- ☒ An ~~initial~~ or substitute computer readable form (CRF) copy of the "Sequence Listing".
- ☒ An ~~initial~~ or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- ☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216

For CRF Submission Help, call (703) 308-4212

For PatentIn software help, call (703) 308-6856

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